AMENDMENTS TO THE CLAIMS

Please amend the claims without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, as follows.

1-24. **(Cancelled)**

25. **(Currently Amended)** An infectivity-enhanced conditionally replicative adenovirus subtype 5 comprising:

(a) a modified fiber protein encoded by the genome of the adenovirus, wherein the modified fiber protein is:

i) an adenoviral fiber protein modified by the presence of a ligand comprising Arg-Gly-Asp in the HI loop of the fiber protein; or

ii) an adenoviral fiber protein modified by replacement of its fiber knob domain with a fiber knob domain from a different subtype of adenovirus;

whereby the ligand or fiber knob domain provides a pathway to cell binding by the modified conditionally replicative adenovirus other than the coxsackie-adenovirus receptor, and thereby enhances infectivity of the conditionally replicative adenovirus in tumor cells over that of wild-type adenovirus;

~~(b) deletion of nucleotides ranging from 324 to 488 of the adenoviral subtype 5 genome; and~~

[[(c)]](b) a tumor-specific promoter driving the transcription of a gene encoding a protein selected from the group consisting of prostate specific antigen, carcinoembryonic antigen, secretory leukoprotease inhibitor, alpha-fetoprotein, vascular endothelial growth factor, CXCR4 or survivin, wherein ~~one or more~~ an early [[genes]] ~~selected from the group consisting of~~ E1~~, E2 and E4 are~~ gene is operably linked to said promoter[[.]]; and

(c) containing a deletion of nucleotides 324 to 488 of the adenoviral subtype 5 genome.

26. **(Cancelled)**

27. **(Previously presented)** The infectivity-enhanced conditionally replicative adenovirus of claim 25, wherein the modified conditionally replicative adenovirus has the modified fiber protein containing the ligand comprising Arg-Gly-Asp in the HI loop.

28. **(Previously presented)** The infectivity-enhanced conditionally replicative adenovirus of claim 25, wherein the modified conditionally replicative adenovirus has the fiber knob domain from a different subtype of adenovirus.

29. **(Previously presented)** The infectivity-enhanced conditionally replicative adenovirus of claim 28, wherein the modified conditionally replicative adenovirus subtype 5 has the fiber knob domain from an adenovirus subtype 3.

30. **(Previously presented)** The infectivity-enhanced conditionally replicative adenovirus of claim 25 wherein the modified conditionally replicative adenovirus provides a pathway to cell binding by the adenovirus other than the coxsackie-adenovirus receptor by containing a ligand, and the ligand has the sequence of SEQ. ID. NO: 1.

31. **(Previously presented)** The infectivity-enhanced conditionally replicative adenovirus of claim 25 wherein the modified conditionally replicative adenovirus is additionally modified by containing and expressing an exogenous nucleotide sequence encoding a therapeutic polypeptide.

32. **(Previously presented)** The infectivity-enhanced conditionally replicative adenovirus of claim 31 wherein said therapeutic gene is a herpes simplex virus thymidine kinase gene.

33. **(Cancelled)**

34. **(Currently Amended)** A method of reducing tumor burden in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a modified human conditionally replicative adenovirus subtype 5 (hAd5) having greater infectivity in tumor cells than wild-type adenovirus, wherein:

the hAd5 contains~~comprises~~ and expresses a chimeric fiber protein, wherein the chimeric fiber protein comprises nucleotide sequence encoding a fiber knob domain from an adenovirus subtype 3, thereby providing a pathway to cell binding other than the coxsackie-adenovirus receptor and enhanced infectivity of the conditionally replicative adenovirus in tumor cells over that of wild-type adenovirus,

further wherein the modified conditionally replicative adenovirus comprises a deletion of ~~ranging from~~ nucleotides 324 to 488 of the ~~E1A promoter~~adenoviral subtype 5 genome, which is replaced by insertion of a promoter region from a gene encoding a protein selected from the group consisting of prostate specific antigen, carcinoembryonic antigen, secretory leukoprotease

inhibitor, alpha-fetoprotein, vascular endothelial growth factor, CXCR4 or survivin, such that replication is more efficient in tumor cells than in most normal cell types.

35. **(Currently Amended)** The method of claim 34 wherein the promoter region is from a gene encoding vascular endothelial growth factor and the modified conditionally replicative adenovirus suppresses tumor growth of non-small cell lung cancer.

36. **(Currently Amended)** The method of claim 34 wherein the promoter region is from a gene encoding vascular endothelial growth factor and the modified conditionally replicative adenovirus suppresses tumor growth of ovarian cancer.

37. **(Currently Amended)** The method of claim 34 wherein the promoter region is from a gene encoding vascular endothelial growth factor and the modified conditionally replicative adenovirus suppresses tumor growth of gastric cancer.

38. **(Currently Amended)** The method of claim 34 wherein the promoter region is from a gene encoding vascular endothelial growth factor and the modified conditionally replicative adenovirus suppresses tumor growth of pancreatic cancer.

39. **(Currently Amended)** The method of claim 34 wherein the promoter region is from a gene encoding vascular endothelial growth factor and the modified conditionally replicative adenovirus does not cause hepatic injury.

40. **(Previously Presented)** The method of claim 34 wherein the modified conditionally replicative adenovirus is additionally modified by containing and expressing an exogenous nucleotide sequence encoding a therapeutic polypeptide.

41. **(Previously Presented)** The method of claim 40 wherein said therapeutic gene is a herpes simplex virus thymidine kinase gene

42. **(Previously Presented)** The method of claim 41 comprising administering to the patient in need thereof an effective amount of the conditionally replicative adenovirus and further comprising administering ganciclovir to the patient.

43. **(Previously presented)** A method of reducing tumor burden in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a modified human conditionally replicative adenovirus subtype 5 (hAd5) having greater infectivity in tumor cells than wild-type adenovirus, wherein:

the hAd5 comprises and expresses a chimeric fiber protein, wherein the chimeric fiber protein comprises nucleotide sequence encoding the fiber knob domain of the canine adenovirus

type 2 thereby providing a pathway to cell binding other than the coxsackie-adenovirus receptor and enhanced infectivity of the conditionally replicative adenovirus in tumor cells over that of wild-type adenovirus,

further wherein the modified conditionally replicative adenovirus comprises a deletion of the E1A promoter, which is replaced by insertion of a tumor-specific promoter from a gene encoding a protein selected from the group consisting of prostate specific antigen, carcinoembryonic antigen, secretory leukoprotease inhibitor, alpha-fetoprotein, vascular endothelial growth factor, CXCR4 or survivin, such that replication is more efficient in tumor cells than in most normal cell types.

44. **(Currently Amended)** The method according to claim 43 wherein the promoter region is from a gene encoding a protein selected from the group consisting of CXCR4 and survivin and the modified conditionally replicative adenovirus suppresses tumor growth of human breast cancer.

45-46. **(Cancelled)**

47. **(Currently Amended)** The method of claim 34, wherein the promoter region is from a gene encoding vascular endothelial growth factor.

48. **(Previously presented)** The method of claim 43, wherein the tumor-specific promoter is from a gene encoding a protein selected from the group consisting of: CXCR4 and survivin.